Amendments to the Specification:

- **On page 47, please replace the paragraph spanning lines 19-27 with the following paragraph:**

Co-immunoprecipitation. For immunoprecipitation assays, Xenopus Smad1 (36), mouse Smad4, and human Smad2 (47), were FLAG-tagged at their C-termini and translated *in vitro* (rabbit reticulocyte extracts; Promega) in the presence of ^{35}S-Met. The FLAG-tagged Smads were bound to anti-FLAG antibody-conjugated beads (Kodak), washed in co-IP buffer (10mM TRIS (*tris*(Hydroxymethyl)aminomethane), pH 7.5, 90 mM NaCl, 1 mM EDTA, 1% ~~Triton X-100~~ TRITON X-100, 10% glycerol, 1 mM phenylmethylsulfonylfluoride) then incubated with ^{35}S-Met-labelled Smurf1 in the same buffer. After washing in co-IP buffer and elution in gel loading buffer, proteins were separated by SDS-PAGE and visualized by autoradiography.

- **Please replace the two (2) paragraphs spanning page 48, line 16 - page 49, line2 with the following two paragraphs:**

Pulse Chase Analysis. COS-1 cells were transfected as indicated above. Two days post-transfection, the cells were labelled for 10 min. at 37° C with 50 μCi [^{35}S]-methionine/ml in methionine-free DMEM (Pulse). Cell layers were then washed two times and incubated in DMEM+10% FCS for the indicated time periods (Chase). At each time point of the chase, cell lysates prepared in TNTE lysis buffer (50 mM TRIS/HCL, pH 7.4, 150 mM NaCl, 0.5% ~~Triton X-100~~ TRITON X-100 and 1 mM EDTA) containing protease and phosphatase inhibitors were subjected to immunoprecipitations using an anti-Smad1 polyclonal antibody. Immune complexes were resolved by SDS-PAGE and visualized by autoradiography. A phosphorimager (Molecular Dynamics) was used to quantitate the amount of metabolically labelled Smad1 present at each time point.

Ubiquitination Assay. 293 T cells were transfected with HA-tagged ubiquitin, untagged-Smad1, and either FLAG-hSmurf1 or FLAG-hSmurf1 (C710A) as indicated above. Two days post-transfection, cells were lysed and subjected to a Smad1 immunoprecipitation. The immunoprecipitates were then washed sequentially two times each in TNTE + 0.1%

~~Triton~~ TRITON X-100, SDS-RIPA (TNTE lysis buffer, 0.1% sodium dodecyl sulfate and 1% deoxycholate), and 500 mM LiCl, 50 mM TRIS/HCL, pH 7.4 and 0.1% ~~Triton~~ TRITON X-100. The presence of HA-ubiquitinated Smad1 in the immune complexes was visualized by SDS-PAGE followed by immunoblotting with the monoclonal anti-HA 12CA5. Protein levels of untagged Smad1, FLAG-hSmurf1 and FLAG-hSmurf1 (C710A) were analyzed by immunoblotting aliquots of total cell lysates with the appropriate antibodies.

- **Please replace the paragraph spanning page 59, line 14 - page 60, line 2 with the following paragraph:**

Immunoprecipitation, Immunoblotting, and Affinity-labelling. For studies in mammalian cells, 293T and COS-1 cells were transiently transfected using calcium phosphate precipitation, or the DEAE-dextran method, respectively. Immunoprecipitation and immunoblotting were carried out using anti-HA monoclonal (12CA5, Boehringer), anti-HA rabbit polyclonal (Santa Cruz), anti Myc monoclonal (9E10 ascites, Developmental Studies Hybridoma Bank), anti-FLAG M2 monoclonal (Sigma) or anti-Smad7 rabbit polyclonal antibodies. For anti-Smad7 antibodies, rabbits were immunized with bacterially-produced GST-Smad7 encoding amino acids 202-260. After absorption of the antibody to either protein G or A-Sepharose, the precipitates were washed five times with TNTE 0.1% (50 mM TRIS, pH 7.4, 150 mM NaCl, 1 mM EDTA, 0.1% ~~Triton X-100~~ TRITON X-100), separated by SDS-PAGE, transferred to nitrocellulose and immunoblotted with the appropriate antibody. Detection was conducted using the appropriate horseradish peroxidase (HRP)-conjugated sheep anti-mouse or anti-rabbit secondary antibodies and enhanced chemiluminescence (Amersham). Bacterially-produced His-Smad7-HA was incubated with either Ni^{2+}-NTA beads (Qiagen) or with GST or GST-Smurf2-bound glutathione beads (Amersham), washed three times with TNTE (0.5% ~~Triton X-100~~ TRITON X-100) and precipitates were analyzed by immunoblotting with anti-HA antibodies. For affinity-labelling, transfected COS-1 cells were incubated with 250 pM [^{125}I]TGF-b1 at 4°C for 1 h, and receptors were cross-linked to ligand with DSS as described (70). The amount of TβR1 bound to Smurf2 or Smad7 was quantified by phosphoroimaging (Molecular Dynamics).